PCT WORLD INTELLECTUAL PROPERTY ORGANIZATION
International Bureau

INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(51) International Patent Classification 5 :
A61C 8/00, A61F 2/28
A61L 31/00

A1

(11) International Publication Number: WO 94/03121

(43) International Publication Date: 17 February 1994 (17.02.94)

(21) International Application Number: PCT/SE93/00657

(22) International Filing Date: 5 August 1993 (05.08.93)

(30) Priority data:
926,604 5 August 1992 (05.08.92) US

(71) Applicant *(for all designated States except US)*: GUIDOR AB [SE/SE]; Novum, Blickagången 6 D, S-141 52 Huddinge (SE).

(72) Inventor; and
(75) Inventor/Applicant *(for US only)* : LUNDGREN, Dan [SE/SE]; Askims Kyrkväg 5, S-436 51 Hovås (SE).

(74) Agents: STRÖM, Tore et al.; Ström & Gulliksson AB, P.O. Box 4188, S-203 13 Malmö (SE).

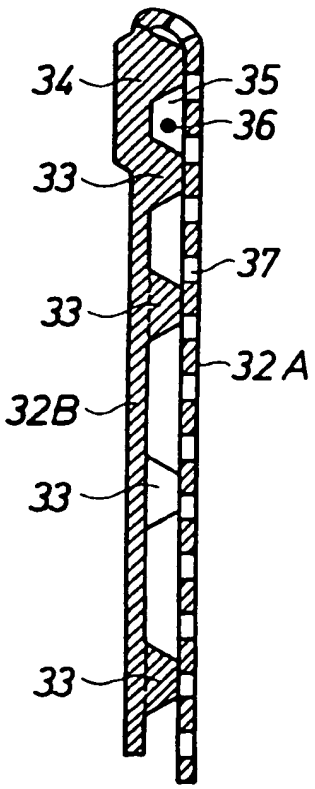
(81) Designated States: AU, CA, FI, JP, NO, US, European patent (AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE).

Published
With international search report.

(54) Title: SURGICAL ELEMENT AND METHOD FOR SELECTIVE TISSUE REGENERATION

(57) Abstract

A surgical element for guided and controlled tissue regeneration and method for selective tissue regeneration. The elements disclosed include embodiments containing ligature arrangements for anchoring the element to a tooth and spacer means on at least one side of the element for separating the implanted element from an adjacent surface, and other embodiments comprising multiple layers of element material with internal spacer means separating the layers. Also disclosed is a method for treating supporting tissues, the method comprising the use of a surgical element for selected influence on the growth of bone.



FOR THE PURPOSES OF INFORMATION ONLY

Codes used to identify States party to the PCT on the front pages of pamphlets publishing international applications under the PCT.

AT	Austria	FR	France	MR	Mauritania
AU	Australia	GA	Gabon	MW	Malawi
BB	Barbados	GB	United Kingdom	NE	Niger
BE	Belgium	GN	Guinea	NL	Netherlands
BF	Burkina Faso	GR	Greece	NO	Norway
BG	Bulgaria	HU	Hungary	NZ	New Zealand
BJ	Benin	IE	Ireland	PL	Poland
BR	Brazil	IT	Italy	PT	Portugal
BY	Belarus	JP	Japan	RO	Romania
CA	Canada	KP	Democratic People's Republic of Korea	RU	Russian Federation
CF	Central African Republic			SD	Sudan
CG	Congo	KR	Republic of Korea	SE	Sweden
CH	Switzerland	KZ	Kazakhstan	SI	Slovenia
CI	Côte d'Ivoire	LI	Liechtenstein	SK	Slovak Republic
CM	Cameroon	LK	Sri Lanka	SN	Senegal
CN	China	LU	Luxembourg	TD	Chad
CS	Czechoslovakia	LV	Latvia	TG	Togo
CZ	Czech Republic	MC	Monaco	UA	Ukraine
DE	Germany	MG	Madagascar	US	United States of America
DK	Denmark	ML	Mali	UZ	Uzbekistan
ES	Spain	MN	Mongolia	VN	Viet Nam
FI	Finland				

SURGICAL ELEMENT AND METHOD FOR SELECTIVE TISSUE REGENERATION

The present invention relates to element and method for selective regeneration of any tissues in a living human or animal body subjected to healing and where these tissues, preferably, should or unconditionally must be favored or unfavored in relation to each other with regard to time and/or location and space during healing of wounds in which specifically ordered tissue formation is aimed at. The element and method of the present invention are applicable within several areas throughout the whole body in situations where selected regeneration of the different tissues participating in the wound healing process is desired.

More particularly, the present invention relates to an element for guided or controlled tissue regeneration to be utilized for selected influence on the healing process during regeneration of supporting tissues adjacent to teeth and dental implants, as well as, during healing after periapical surgery. However, in addition to the periodontal application, any bone or bone area throughout the whole body available for surgical intervention can be treated by using the method and element of the present invention to control bone fill of bone cavities resulting from cysts and malformations and of diastases following bone fractures.

The aim of the treatment may be a predictable filling out of bone defects of different sizes and shapes in the edentulous jaw bone or adjacent to teeth or bone-anchored implants, as well as bone defects anywhere else

within the body as in the maxillofacial bones, in the skull bones, in the long bones, in the hand and foot bones, and in the back bones. The defects may have well-defined borderlines or successively pass into the surrounding bones and their bottom and wall surfaces can contain more or less of compact (cortical) bone. The defects may be so narrow so they rather would be defined as bone depressions than bone defects. In fact, there are many sites where the bone surface to be chosen for regeneration is flat or convex rather than concave, but where there are strong indications for building up rather than filling out bone. The bone defect can also include a fracture with more or less advanced discontinuity. Furthermore, the defect can be of the through-type, as is the case with some skull bone and jaw bone defects. The present invention may also be used in situations where there are indications for elongation (or shortening) of bones, for instance, of jaw bones and long bones. The technique can be used to collect bone for transplantation.

There are many causes of the above-described bone defects, such as congenital defects, traumatic lesions, defects caused by tooth extractions, osteitis, cysts, tumors, periodontal destructions, bone resorptions due to overloading, infections or internal diseases. These defects may be functional and/or aesthetic in nature. Other therapeutic measures might be based solely on aesthetic indications for correction of deformities or aesthetic "improvements" of the appearance. Many of the mentioned indications will be elucidated and described in detail below in conjunction with the different embodiments and exemplifications.

There are still other areas of indication within the human or animal body for the technique of the present invention, such as selective regeneration of more or less

specialized tissues, for example, membranes demarcating body cavities and/or separating different tissues and organs from each other, as well as, for selective regeneration of different tissues within the organs, of the organs themselves in relation to the surrounding tissues, or of nerves. Examples of membranes are the periosteum, the membrane of the brain, and the peritoneal membrane; while examples of organs are the liver, the throat, the ventricle, the kidney, the heart, and the pancreas. Also, muscle tissue and tendons should be possible to regenerate with the element of the present invention.

Application of the concept of controlled tissue regeneration, preferably, on reformation or new formation of bone tissue, briefly means that the space to be filled with the bone tissue must be available for the bone-forming cells at the same time that it must be separated from the non-desired tissues, for instance, soft tissues such as connective tissue and epithelium. It should be clearly understood that the bone-forming cells (osteoblasts) are residing mainly along the endosteal surfaces of the spongious (cancellous) bone. It is, therefore, important to assure the best possible communication between the endosteal surfaces and the space to be filled with bone. This means that compact bone, which covers the spongious bone and blocks the communication should, at least in part, be removed to optimize the ingrowth of these cells into the space. It is advisable to first remove all soft tissue within the space in question. Perforations in the form of round holes or slots should be made through the remaining compact bone to insure that there is as much direct connection as possible between the space and the spongious bone.

The soft tissues must be kept out of the space by a convenient means from the very beginning of the wound healing process. This means should reliably preclude ingrowth of soft tissue cells through itself or via any lateral space between the element and the surrounding bone. If the space is more or less occupied by soft tissue, a complete occupation of the space by bone tissue will be prevented.

An element to be successfully used for guided bone tissue regeneration should therefore:

1) be constructed to insure that soft tissue cells cannot pass the element or that ingrowth of soft tissue cells into the element is delayed to such an extent that the bone tissue regeneration in the desired space is not jeopardized;

2) be constructed to prevent the ingrowth of soft tissue between the element and the bone surrounding the space or between the element and an endosseous implant;

3) be able to maintain the space to be filled;

4) permit transport of bone cells via the perforations lateral to the bone space into the space to be filled;

5) be constructed to provide the best possible stability of the tissue as well as the element;

6) minimize the risk of rupture of the soft tissue flap covering the wound area; and

7) preferably be biodegradable in such a way that eventually it will disappear during the healing process without adverse effect on the organism.

WO 90/07308 discloses an element for controlled tissue regeneration which can be placed within a desired area of the body in such a way that a predictable healing sequence is achieved by the element predictably creating space for regeneration of tissue.

This prior art element comprises at least one member having opposite sides, and at least one spacer means for separating said member on at least one side thereof from an ajacent surface.

The invention relates to an element of this kind and provides new and useful improvements thereof.

In periodontal use, there should be secured in the cervical (tooth-neck) region a tight anchorage (retention) of the element against the root surface. This is achieved in the prior art element for the periodontal use by said element having a ligature for anchoring the ligature to the tooth. According to one aspect of the present invention the element comprises anchoring means for the ligature engaging the ligature at positions spaced longitudinally of the ligature.

According to a second aspect of the invention the separating means of the element, separating the element from adjacent tissue such as bone tissue, a root surface, or soft tissue, or separating adjacent sheets forming parts of a multiple sheet element, comprises a mesh, a net, or a knitted, woven or non-woven fabric.

According to a third aspect of the invention the element forms a self-supporting central portion and a marginal portion surrounding said central portion, for sealing engagement with a bone surface surrounding a bone defect covered by said central portion.

The present invention also provides a method for creating selected healing process in connection with tissue regeneration, wherein a defined space for tissue growth is provided between an implanted element and adjacent tissue. The space can be maintained by means of spacers on the element, but the element itself may also have sufficient inherent shape stability so as to maintain the space without spacers being provided.

The element should, preferably, include a totally biodegradable material but could also include a partly biodegradable or a non-biodegradable material. It has been found that the material of the element should not be too reactive in its resorption behavior and should retain its dimensional integrity, at least partially and at least during the first four weeks in vivo after implantation. In addition, the material should induce only mild tissue reactions. Thus, any effects due to degradation of the element, preferably, should not start earlier than 4 to 6 weeks after the surgical implantation resulting in an initial period of healing free from disturbances. Also, after the beginning of the degradation of the element, the tissue effects should be minimal.

Suitable biodegradable materials include polymers such as polyglycolide (PGA), polylactide (PLA), stereocopolymers of PLA, copolymers of PLA, and degradable ceramic materials. Other examples are hyaluronic acids and mixtures of the mentioned materials.

Still other examples are polydioxanone, polyhydroxy butyric acid, copolymers of polyhydroxy butyric acid and hydroxy valeric acid, and polyesters of succinic acid, and silicones.

Suitable non-biodegradable materials could be, but are not limited to, polyurethanes, polyesters, expanded polytetrafluorethylene and combinations of these materials.

The elements should be very thin and, preferably, the maximum thickness of a single sheet element or each sheet of a multiple sheet element or material should be 50-300 μm.

The separating means also can include a gel having macromolecular structure applied between the element and

the adjacent surface from which the element should be spaced.

Illustrative embodiments of the invention will be described below reference being made to the accompanying drawings, in which

FIG. 1 is a fragmentary plan view of a sheet for an element of sandwich structure.

FIG. 2 is a vertical-sectional view of the element of sandwich structure obtained by using the sheet of FIG. 1.

FIG. 3 is a vertical-sectional view of a preferred embodiment of the sandwich structure.

FIG. 4 is a fragmentary vertical-sectional view of a tooth with the element of the sandwich structure shown in FIG. 3 mounted on the tooth.

FIG. 5 is a fragmentary plan view of an element showing anchoring means for a ligature,

FIG. 6 is a fragmentary cross sectional view of the element in FIG. 5, taken along the line VI-VI in FIG. 5,

FIG. 7 is a fragmentary vertical sectional view of a tooth with the element of FIGS. 5 and 6 mounted on the tooth,

FIG. 8 is an enlarged fragmentary cross sectional view of the ligature anchoring means of FIG. 5 and 6,

FIG. 9 is a view similar to FIG. 8 of a modified embodiment of the ligature anchoring means,

FIG. 10 is a side view of another embodiment of the ligature anchoring means,

FIG. 11 is a fragmentary cross sectional view with the ligature and the anchoring means of FIG. 10,

FIG. 12 is a side view of a further embodiment of the ligature anchoring means,

FIG. 13 is a vertical cross sectional view of a sandwich type element having spacer means between the

element portions, comprising av mesh or similar structure,

FIG. 14 is a vertical cross sectional view of a sandwich type element wherein one sheet of the sandwich structure comprises a mesh or similar structure,

FIGS 15 and 16 are vertical cross sectional views of elements having spacer means comprising a mesh or similar structure,

FIG. 17 is a fragmentary plan view of a composite mesh structure,

FIG. 18 is a plan view of an element to be used between two adjacent teeth,

FIG. 19 is a view illustrating an embodiment of the element applied to an implant,

FIG. 20 is a view illustrating a another embodiment of the element applied to an implant,

FIG. 21 is a cross sectional view of a bone defect filled with connective tissue,

FIG. 22 is a cross sectional view of the defect in FIG. 21 after a flap has been raised and the connective tissue within the bone defect has been separately removed,

FIG. 23 is a cross sectional view of the same bone defect as in FIGS. 21 and 22, the element of the present invention being placed to cover the defect and the soft tissue flap being replaced and sutured to cover the element,

FIG. 24 is a horizontal cross sectional view of the same defect,

FIG. 25 is a cross sectional view showing an implant partly located outside the bone tissue,

FIG. 26 is a longitudinal cross-sectional view of the implant of FIG. 25,

FIG. 27 is a cross sectional view of the same bone defect as in FIGS. 21 to 24, covered by a further embodiment of the present invention,

FIG. 28 is a horizontal cross sectional view of the same defect as in FIG. 27,

FIG. 29 is a cross sectional view of the same bone defect as described above, with the element covering the defect having three layers,

FIG. 30 is an enlarged fragmentary cross sectional view of the left part of the element in FIG. 29,

FIG. 31 is a plan view of the defect in FIG. 29,

FIG. 32 is a cross sectional view of a domeshaped element according to the invention, and

FIG. 33 is a plan view of the element shown FIG. 32.

Referring to the drawings FIGS. 1 and 2 disclose an embodiment of the present invention which forms a sandwich-type structure made of a sheet 32 of a rectangular or other configuration having two substantially equal portions 32A and 32B shown fragmentarily only in FIG. 1. This sheet is a foil made of a biodegradable polymer material having a thickness, e.g. of about 120-150 μm, and a size, e.g. of about 10 x 20 mm. However, the shape, configuration and dimensions can vary as can the stiffness of the material. The single sheet can have a thickness from 20 μm up to 500 μm. The stiffness can vary from a nonflexible, centrally located core to a completely flexible consistence of the peripheral parts. The different configurations may include ovoid, horseshoe shaped, or skirt shaped foils. The sheet can be produced by compression molding, but other manufacturing methods can be applied, such as calendaring, casting, injection molding, or other techniques. Portion 32B forms at one side thereof protrusions 33 which have the shape of truncated cones

with a base diameter of about 0.4 mm and a height of about 0.2 a 0.3 mm. The protrusions of one row thereof adjacent to portion 32a have a center distance of about 0.6 mm, with the center distance of the remaining rows being about 1.2 mm and the center distance between the rows being about 1.0 mm. At the top, forming the most coronal part of the element when mounted to a tooth, the portion 32A forms a rib or bar 34 extending over the full width of portion 32B and protruding at both sides thereof, said rib or bar being constructed to be tightly applied against the tooth. The rib or bar 34 defines, together with the adjacent protrusions 33, a channel 35 for an anchoring ligature 36 extending through the channel and being displaceable longitudinally or non-displaceable therein.

FIG. 2 discloses a double-sheet element. In the embodiment shown, the sheet of FIG. 1 has been folded to form a double-sheet structure or a laminate, wherein the adjacent surfaces of portions 32A and 32B are spaced by protrusions 33 formed by the portion 32B, at a distance of 0.2 mm to create a free space between said surfaces.

In the embodiment, disclosed in FIG 3, the portion 32B forms at the outside surface thereof protrusions 33A being distributed over the surface in the same configuration as protrusions 33 and having a height of about 0.1 mm. These protrusions are provided to form spacers between the outside surface of portion 32B and the surface of the tooth. Moreover, there are provided small circular perforations 37A having a typical diameter of 70 μm or less and arranged in a hexagonal pattern, wherein the center distance of the apertures is about 0.2 mm, more accurately 0.16 mm. These apertures cover an area of 10 to 30 percent of the surface area.

The two portions 32A and 32B can comprise individually produced separate sheets which are

interconnected at one or more edges and/or at the protrusions 33 to form a sandwich structure or a laminate Moreover, the protrusions 33 can be replaced by other means forming the spacers such as biocompatible materials or combinations of materials with variable degrees of degradation to govern the degradation profile and thereby the ingrowth pattern of tissues. As an example, quickly biodegradable materials such as hyaluronic acid might be blended with more slowly biodegradable polyactide (PLA) components.

FIG. 4 discloses the element of FIG. 3 mounted to a tooth. An incision is made and a mucoperiosteal flap is raised to expose the bone having a defect to be regenerated. It is desirable that the coronal part of the element is placed about 2 mm apical to the gingival margin, following suturing of the flap, in order to facilitate connective tissue ingrowth into the element before it is reached by the apically proliferating gingival epithelium. This will prevent gingival recession and element exposure. However, the position of the anchoring ligature 36, used to attach the element to the tooth, is also determined by the highest point of the alveolar bone level around the tooth. This means that it is not possible to place the coronal aspect of the element apical to this level. As a consequence, it is desired to have the ligature placed as close as possible to the top of the element in order to facilitate optimal flap coverage of the element. This is achieved in the embodiments of FIGS. 1-3. The ligature can be longitudinally displaceable in the channel, which is a convenient feature in the implantation situation, allowing the element to be easily adjusted to the desired position.

However, the ligature can also be attached to the element in a fixed position as shown in FIG. 5 and 6

which disclose an element 32B' the collar portion of which is curved at 100 but which may as well be straight or have any other shape. The ligature 36 is anchored in notches 101 shaped so as to facilitate the positioning of the ligature and to retain the ligature in place. As shown in FIG. 6 the notches are formed by projections 102 and the rib or bar 34' which is of angular shape and forms two surface portions 103 and 104 substantially perpendicular to each other with a curved transition portion 105 therebetween. A second element 32A' is placed on top of the protrusions 33 and the rib or bar 34' formed by element 32B', and is connected thereto so as to form together with element 32B' a sandwich structure or laminate of the type mentioned above, element 32A' covering element 32B' partly or completely.

FIG. 7 discloses the element of FIGS 5 and 6 attached to the root 10' of a tooth 10, and as will be seen the rib or bar 34' preserves at the surface portions 103, 104, and 105 a good sealing effect at the coronal margin independently of the angle between the root surface and the element. Preferably, the rib or bar 34' and the projections 102 is made of a resiliently deformable material which can adapt itself to the ligature when this is pressed into the notches 101 as shown in FIG. 8, or the notch can be formed as an undercut notch as shown in FIG. 9 having an opening narrower than the diameter of the ligature so that the material will yield resiliently when the ligature is pressed into the notch and the ligature will be retained therein by snap action but will be free to move in relation to the element allowing adjustement of the ligature.

A further embodiment allowing adjustement of the ligature is shown in FIG. 10 according to which the ligature 36 is housed in a helically bent strip 106

having circular or rectangular cross sectional shape. The helical strip can be bent to the desired form and attached to the element by welding, gluing or in any other manner or can be retained in the the channel 35 formed by the rib or bar 34, FIGS. 2 and 3, as shown in FIG. 11, or in the notches 101. In a still further embodiment the ligature is enclosed in a tube 107, FIG. 12, having slots 108 allowing bending of the tube which can be secured to the element in the same manner as mentioned in connection with the helical strip.

A further advantage inherent in the ligature channel is that it facilitates the placement of two elements, if desired, on a tooth with the same ligature. It also provides the option of, at the point of surgery, separating a part of an element from the rest with the purpose of placing this separated part on another location of the treated tooth in question. Such separation may also facilitate intra- and supra-defect application of the element inside the defect, and application of the element laterally to the defect, respectively. The rib or bar 34A aims at sealing the coronal margin of the element to the root surface to prevent gingival tissue downgrowth between the element and the root surface. As this bar is located in the region of the ligature channel, it also serves as reinforcement to prevent rupture of the device via the anchoring ligature.

Central to the periodontal application of the guided tissue regeneration concept is the prevention of gingival connective tissue and epithelium making contact with the root surface during healing. The sandwich structure of FIG. 3 is ideally suited to accomplish this objective. During the healing process after the element has been implanted, gingival connective tissue will easily penetrate the proportionally large rectangular

perforations 37 of the external layer 32B, facing the gingival flap, and then spread out in the space between the two layers 32A and 32B. A biological "element" is thus formed that prevents downgrowth of gingival epithelium along the wound surface facing the element. As a consequence, gingival recession and element exposure are prevented. The outcome of the competition between apical migration of the gingival epithelium and connective tissue ingrowth into the sandwich structure will, to some extent, be dependent upon the distance the epithelium has to migrate before reaching the coronal aspect of the element. This means that, during initial healing, minor epithelial downgrowth may sometimes occur at the most coronal part of the wound preceding the connective tissue ingrowth. However, since connective tissue ingrowth is permitted through the perforation of the entire length of the external wall, the epithelial migration will always be prevented somewhere along the extension of the element.

Conventional devices for guided tissue regeneration often collapse into close contact with the treated root surface after implantation, thus blocking the space between the root and the device that is desired for ligament regeneration. The spacers 33A on the internal layer 32B prevent any such collapse, thereby assuring the space needed for the regeneration of the periodontal ligament.

The space between the two layers forming the sandwich structure or the space provided between the element and the root surface or the bone surface can also be more or less occupied by a three dimensional mesh or similar structure. In FIGS. 13 - 16 there are shown several embodiments utilising a knitted or woven mesh or nonwoven fabric as spacer means.

In FIG. 13 there is shown a sandwich structure formed by a folded element wherein the space between the two portions 32A and 32B is maintained by a mesh 109, the space between the element and the root or bone surface being maintained by protrusions 33A.

FIG. 14 discloses a sandwich structure comprising a portion 32B formed by a sheet of the construction shown in FIG.3, wherein the portion 32A is replaced by a mesh 110. The mesh allows integration of the implanted element with surrounding tissue.

Further embodiments are shown in FIGS. 15 and 16. In FIG. 15 sheet 32 having smooth opposite sides is provided with meshes 111 and 112 on both sides, and in FIG. 16 only one side of the sheet 32 is provided with a mesh 112, the other side of the element having protrusions 33A.

The mesh or meshes can be attached to the element or the portions thereof, respectively, by melting, ultrasonic welding, disolution of surface layers, or by gluing. The mesh can comprise a single layer or several layers as is necessary in order to provide the desired spacing. FIG. 17 discloses two loosely woven meshes 113 and 114 which are placed one on top of the other and are slightly displaced to form spaces for tissue integration of the desired size.

A preferred embodiment for regenerative treatment of interproximal periodontal defects is a double-curved element 21', as shown in FIG. 18, designed to have a close fit to the proximal root surfaces of two adjacent teeth, as indicated at 10A and 10B by dash-and dot lines. Measurements of the distance between the proximal root surfaces of adjacent teeth with normal proximal contact relationships show that this distance may vary considerably at the cementoenamel junction, as well as, more apically. The element should, therefore, be designed

to have a width which may vary from 1 to 10 mm, preferably, from 3-7 mm, at its most narrow site. However, if the material is in a malleable state at body temperature, this distance can be increased at least between 25 and 50 percent by stretching the element to secure a tight adaptation to the proximal root surfaces in each individual case. This embodiment may include spacers integral with the element (protrusions), or may be combined with separate spacers (mesh or fabric) to avoid collapse of the element into the periodontal defect. The element can also be reinforced by fibers or ridges or be provided with a harder core to avoid collapse. The ligature anchoring means can be constructed as described above.

FIGS. 19 and 20 disclose embodiments of the present invention in connection with an implant 45 In these embodiments, the element 21 is clamped between a cap 46, which is secured into the implant end surface by means of a screw 47, screwed into the implant, together with an underlying member 48, which may be formed as a disc, a net, a star, or a spider. This member is stiff enough to support the element, so that it will be held spaced from the bone 12 covering a bone defect 11. Member 48 may be made of metal, or plastic material, at least in part resorbable or non-resorbable, which can be plastically deformed at room temperature or at an elevated temperature, so that it may be adapted to the desired form of the element as shown to the right in FIG. 20, wherein member 48 has been bent down so that the element extends substantially vertically to cover a space 49 to be restored by bone tissue growth thereinto.

FIG. 21 shows a cross-sectional view of the center of a bone defect or a bone cavity 50 filled with soft (connective) tissue 51 in turn being covered by epithelium 52. The spongious or cancellous bone

surrounding the bone defect is indicated at 53 and the compact or cortical bone which covers the spongious bone indicated at 54. The compact bone, in turn, is covered with a thin membrane, the periosteum 55. By the aid of a surgical scalpel 56, an incision 57 is made through the soft tissue, including the periosteum 54, down to the compact bone to raise a mucoperiosteal flap 58 as shown in FIG. 22, which is showing the same view and section as FIG. 21. The flap is trimmed in that the soft tissue occupying the bone defect 51 is cut away from the rest of the flap 58.

FIG. 23 shows the same view and section as shown before in FIGS. 21 and 22, and FIG. 24 shows a horizontal-sectional view of the same defect. An element of the present invention 59 has been placed to cover the bone defect containing a blood clot and bone cells. The element has the form of a plate, sheet, or lamina consisting of a material which, preferably, is bioresorbable. The material might, preferably, be so stiff that the element is able to maintain its shape long enough for the critical guided healing to occur even when it is subjected to loading from the surrounding tissues and the extracorporeal environment. The element is easy to reshape, especially when warmed up. It is provided with protrusions 60 which function as spacers or stand-offs between the plate-formed part of the element and the bone. Those protrusions indicated at 60', which are located in the border line area between the bone defect and the surrounding bone surface, are especially important as they secure a space between the openings of perforations 61, which are made as slots or holes through the compact bone into the spongious bone to secure migration of the bone-producing cells residing in the spongious bone into the bone defect. These perforations are especially important when the bone defect is more or

less occupied by an implant, as will be described later on. The slots or holes are made by means of burs, sharp hand instruments, or laser equipment, and should also include perforations 62 of the walls of the defect itself. One or several of the protrusions, indicated at 63, can in certain embodiments of the present invention be very long (5-25 mm) and stiff to assist in the support of the element, especially if the element is made thin and wide and, therefore, is less able to maintain its shape and location without beam support.

A small zone 64 of the element, immediately peripheral to the zone corresponding to the border line perforations, should be in tight junction with the bone surface to prevent ingrowth of connective tissue between the element and the bone which will jeopardize the bone healing of the defect. Peripheral to this occluding zone, the element, preferably, should be so perforated that only a minor part of this area 65 consists of element material, meaning that the connective tissue and/or the periosteal tissue of the flap 58, immediately after the replacement of the flap to cover the element, will come in close contact with the bone surface in a clotting/gluing relationship to secure an attachment with the bone which very soon will be reinforced by ingrowth of cells 66 joining the two types of tissue.

Alternatively, the element can be made wide with protrusions extending from the inner layer towards the bone defect and peripheral bone crest. Bone-producing cells can then migrate into the area created by the protrusions between the element and the bone; such bone cell migration is particularly effective if bone bleeding and blod clot formation is secured by perforating the cortical wall, e. g. using a small round burr, to give spongious bone easy access to the area. Hence, this bone

cell migration will block the possibility for ingrowth of gingival tillue into the bone defect from the periphery.

FIG. 25 is a cross-sectional view of an implant 67 in part submerged in the bone tissue 53. An element 59, of essentially the same embodiment as described in FIGS. 23 and 24, covers the implant and the bone surrounding the implant. The soft tissue to cover the element is not shown. FIG. 26 is a longitudinal sectional view showing the denuded part of the implant with the element covering the implant and the surrounding bone. The double role of the protrusions is obvious: first to create space 68 for the entrance of bone producing cells from the spongious bone area; and second, to create and maintain the space 69 between the element and the implant within which bone is to be formed.

FIGS. 27 and 28 show the same situation and views as FIGS. 23 and 24. The soft tissue flap 58 is repositioned but is not yet in its final position. This embodiment of the element has two layers, 59A and 59B, instead of one as in FIGS. 23 and 24. The fact that both layers are provided with protrusions, means that the size and location of such protrusions regulate not only the space between the inner layer and the bone, but also the space 70 between the outer and inner layers. In addition, both the outer and the inner layer are perforated with at least one perforation, preferably, not larger that 100 μm.

There are at least two reasons why the element, preferably, should be provided with perforations. First, there are indications that transport of body fluids from the soft tissues to the hard (bone) tissues and vice versa is of benefit both for the soft and hard tissue nutrition and, thus, for the rate, safety, and predictability of the healing, perforations allow ingrowth of tissue into the element, which stabilizes not

only the element, but also the tissue flap in the intended position. This in turn counteracts the risk of rupture of the suture line or the flap tissue. Thus, the healing procedure is facilitated. In the embodiment shown in FIGS. 27 and 28, the location of the perforation or perforations of the outer layer is within the center of the element as indicated at 71, i.e., close to, or, preferably, quite above the holes or slots in the bone lateral to the defect. This means that the transport of body fluids between the soft and hard tissue compartments is maintained during the entire wound-healing phase at the same time as the migration of continuous cell populations from the connective tissue to the bone defect is substantially delayed due to the long distance from the first connective tissue cell entrance 71 to the entrance into the bone defect 72. The central importance of the lateral perforations 61 is now obvious not only when the bone defect is occupied by an implant but in any situation, because the delivery of bone cells from these perforations means that the bone matrix front advancing toward the defect center already has passed and blocked the peripherally-located perforations of the inner element layer for connective tissue cells. As is shown in FIG. 27, the protrusions can be arranged in a continuous circumferent order as indicated at 73, resulting in a complete compartmentalization of the central perforations of the outer layer subject to one or more perforations 74 through this continuous beam. This arrangement further markedly delays the ingrowth of connective tissue cells into the bone defect, thereby increasing the chance for predictable guided bone regeneration.

A further embodiment of the element is shown in FIGS. 29 to 30. It can be seen that a third element layer 59C has been added, the outermost layer 59C having lateral perforations, while the middle layer 59B has a

central perforation 71, and the innermost layer 59A has lateral perforations 76. Thus, the distance for cell migration is further increased. As is shown in FIG. 31, also the arrangement of another circumferent protrusion 77 may help to further delay the connective tissue cell migration.

FIGS. 32 and 33 disclose a still further embodiment of the element according to the invention for the treatement of a bone defect. In this embodiment an element 115 of a malleable material as referred to in connection with the embodiments previously described has protrusions 116 on one side of the element. The element is perforated, the perforations having a diameter of about 200 to 300 μm. Against the central portion of element 115 there is attached a perforated or non-perforated element 117 of a resorbable polymer or polyester like polyglycolide, polylactide, polycaprolactene or polydioxanone, which forms a dome and imparts to the central portion of element 115 a corresponding dome shape. Element 117 forms a brim 118 which is connected by welding or by any other conventional method to a ring 119 of malleable material which can be the same as that of element 115. The ring 118 can be perforated or unperforated.

In use the composite element of FIGS. 32 and 33 is applied over the bone defect the ring 119 being sealingly engaged with the bone surface around the bone defect which is covered by the domeshaped central portion defined by element 117.

In a modification element 117 comprises a net structure preferably forming hexagonal openings. The openings of the net and the openings of a perforated element 117, respectively, allow body liquid and nutrients to penetrate into the bone cavity, surrounding tissue being prevented to grow into the bone cavity by

the tight seal provided at the ring 119 sealingly engaging the bone surface around the cavity.

Thus, it is possible, within a broad range, to influence the rate of ingrowth of different cell types into a wound area aimed for guided tissue regeneration by varying the placement of element layers in relation to the defect, the space between the layers, and the size and location of layer perforations.

The element of the present invention can be constructed in ways other than those described with reference to the drawings. It is also possible to provide elements of any type with active substances such as pharmaceutical or biochemical substances of the kind referred to herein.

In order to further illustrate the present invention, reference is made to the following examples of the preferred embodiment, based on experiences from guided tissue regeneration procedures (GTR-procedures).

Exampel 1

Following mucoperiosteal flap elevation, recession-type defects (72 teeth) and interproximal defects (24 teeth; 40 defects) were created in 12 monkeys (Macaca Fascicularis). At each of the experimental sites, an element according to FIG. 3, having protrusions 33 with a length of 200 μm, perforations 37 with a diameter of 300 μm, protrusions 33A with a length of 200 μm, and perforations 37A with a diameter of 70 μm, was placed to cover the defect. The flaps were then repositioned and sutured to complete coverage of the element.

After a healing period of 1, 3, 6, and 12 months, the animals were sacrificed and the experimental teeth were dissected free and placed in 10 percent buffered formalin. The specimens were decalcified and embedded in

paraffin. Buccolingual sections (recession type defects) and mesiodistal sections (interproximal defects) of each root were prepared with a microtome set at 3-5 μm, stained with Haematoxylin-eosin or Mallory's connective tissue stain, and subjected to analysis in a light microscope.

Around all teeth, healing occurred with minimal gingival inflammation and recession. Element exposure was observed at 5 of the 72 recession type defects and at 4 of the 40 interproximal defects. No element was rejected during the healing period, which varied from 1 to 12 months.

1-month histological observation: The element was completely integrated with the soft tissue of the gingiva, and connective tissue fibers were seen penetrating into the matrix. The apical extension of epithelial downgrowth terminated coronal to the border of the element and no epithelial cells were seen along the element. No inflammatory cell infiltrates were present, however, solitary macrophages and multinuclear foreign body giant cells were observed adjacent to the element material. New attachment had formed to a level corresponding to the coronal margin of the element.

3-month histological observation: New attachment was present along the entire root portion covered by the element. At this time bone regeneration was more pronounced. In some specimens, new bone had formed also within the element, thus, illustrating the biocompatiblity of the element material. Functionally oriented periodontal ligament fibers were seen extending from the newly formed cementum to the newly formed bone and the adjacent gingival connective tissue. Overt signs of element fragmentation were seen in all specimens. As in the 1-month observation, only solitary inflammatory cells were seen adjacent to the

element material.

6 and 12 month histological observation:

Extensive amounts of new attachement and new bone had formed. No element material was seen, indicating complete degradation of the element.

It can be concluded that:

- the use of the element of the present invention in GTR-procedures resulted in extensive formation of new attachment and new bone;

- the integration of the element with the soft tissue flap during the initial healing minimized epithelial downgrowth, gingival recession, and element exposure; and the element was completely degraded within 6 to 12 months after surgery.

Example 2

The study comprised 32 defects (12 furcational and 20 non-furcational defects) in 18 patients referred to specialists in periodontology for the treatment of advanced periodontal disease. All patients participated in the study on a voluntary basis. Following the initial examination and informed consent, each patient was given detailed instruction in plaque control measures.

Following flap elevation, sealing, root planing and removal of granulation tissue, a biodegradable element, as that in Example 1, was adjusted to cover the defect. The coronal portion of the element was tightly adapted to the tooth-neck by a degradable sling suture. The flaps were repositioned and secured with interdental sutures to complete coverage of the element. The sutures were removed after 2 weeks. Following surgery, the patients were instructed not to perform mechanical plaque control at the surgical sites but to rinse the mouth with a 0.2 % chlorhexidine digluconate solution (Hibitane®, ICIPharma, Gothenburg, Sweden) twice daily for one

minute. The mouth-rinse regimen was continued for 4 to 6 weeks. Self-performed mechanical plaque control was re-initiated 3 to 4 weeks after surgery. During the period surgery, the patients were maintained on a plaque control program which included professional tooth cleaning once every 2 weeks. During the subsequent 3 month period, the patients were recalled for the same plaque control program once every 4 weeks. No subgingival instrumentation was performed at any recall visit.

At the day of surgery, and 6 months after surgery, the following variables were assessed:

1. Gingival position: The distance from gingival margin to CEJ.

2. Probing pocket depth (PPD).

3. Probing attachment level vertically (PAL-V) using CEJ or other landmarks on the tooth as reference points.

4. Probing attachment level horizontally (PAL H) for furcational defects.

Measurements were performed using a probe calibrated in mm, and recorded to the nearest mm.

The results are summarized in Table 2 (furcational defects), and Table 1 (non-furcational defects), below.

At the furcational defects, mean PPO was reduced from 5.9 to 3.0 mm. The mean gain of PAL-V was 3.2 μm and the mean gain of PAB-H was 3.1 mm, resulting in complete closure of 2 of the 12 defects. The remaining 5 furcational defects were converted to degree I involvement. The position of the gingival margin was unchanged or coronal to the presurgical level at 9 of the 12 furcational defects. Gingival recession had occurred only at 2 furcational defects.

At the non-furcational defects (Table 1), mean PPD was reduced from 8.9 to 3.1 mm. The mean gain of PAL amounted to 4.9 mm. Mean gingival recession amounted to 1.0 mm. The position of the gingival margin was unchanged or coronal to the presurgical level at 9 of the 20 infrabony defects. The gingival recession of the remaining 11 defects was on the average 2.4 mm (range 1-5 mm).

Based on the results of this study, it is concluded that the use of the biodegradable element of the present invention in GTR-procedure will result in pronounced gain of attachment.

Example 3

The study comprised 32 defects (12 furcational and 20 non-furcational defects) in 18 patients referred to specialists in periodontology for the treatment of advanced periodontal disease. All patients participated in the study on a voluntary basis. Following the initial examination and informed consent, each patient was given detailed instruction in plaque control measures.

Following flap elevation, scaling, root planing, and removal of granulation tissue, a biodegradable element, as that in Example 1, was adjusted to cover the defect. The coronal portion of the device was tightly adapted to the tooth-neck by a biodegradable sling suture. The flaps

were repositioned and secured with interdental sutures to complete coverage of the element. Sutures were removed after 2 weeks. Following surgery, the patients were instructed not to perform mechanical plaque control at the surgical sites but to rinse the mouth with a 0.2 % chlorhexidine digluconate solution (Hibitane®, ICIPharma, Gothenburg, Sweden) twice daily for one minute. The mouth-rinse regimen was continued for 4 to 6 weeks. Self-performed mechanical plaque control was re-initiated 3 to 4 weeks after surgery. During the period of 3 months after surgery, the patients were maintained on a plaque control program which included professional tooth cleaning once every 2 weeks. During the subsequent 3 month period, the patients were recalled for the same plaque control program once every 4 weeks. No subgingival instrumentation was performed at any recall visit.

The qingival position was assessed prior to, and 6 months after, surgery.

The following variables were recorded at 2 weeks, and at 1, 3 and 6 months after surgery:

1. Gingival condition, Index 0-3:

0 = Healthy, non-inflamed soft tissue at the element covered area.

1 = Inflamed gingival margin, but predominantly healthy soft tissue at the element covered area.

2 = Soft tissue with general redness along the element covered area, but with no swelling and/or suppuration.

3 = General redness, swelling and/or suppuration.

2. Exposure of element (mm) in apical direction. The results are summarized in Table 2 (furcational defects) and Table 1 (non-furcational defects), below.

Clinical signs of inflamation (Index 2) in the soft tissue covering the element was found adjacent to only 1 defect and was limited to the first month of healing. The position of the qingival margin was unchanged or coronal to the presurgical level at 10 of the 12 furcational defects and at 9 of the 20 non-furcational defects. The gingival recession of the remaining 13 defects was on the average 2.2 mm (range 1-5 mm). Element exposure occurred at 5 of the 32 defects.

The very low incidence of gingival pathology, gingival recession, and element exposure, illustrates the biocompatibility and safety of the element of the present invention.

SUBSTITUTE SHEET

Table 1. Clinical assessments of 20 treated teeth (non-furcational defects) in 18 patients. 6-month Evaluation

	Patient	Sex	Age	Tooth	Gingival Condition Index (0-3)					Exposure of device (mm)					PPD Initial	PPD Residual	PAL Gain (mm)	Position of Gingival Margin* (mm)
					2w	1m	2m	3m	6m	2w	1m	2m	3m	6m				
1	K-G. S.	Male	45	13	2	1	0	0	0	0	0	0	0	0	6	1	6	1
2	G.B.	Male	46	11	0	0	0	0	0	0	0	0	0	0	12	1	9	-2
3	S.F.	Female	54	33	0	0	0	0	0	2	0	0	0	0	12	1	9	-2
4	S.Å.	Male	62	43	0	0	0	0	0	0	0	0	0	0	6	1	6	1
5	S.L.	Male	65	13	0	0	0	0	0	0	0	0	0	0	9	5	4	0
6	S.L.			21	0	0	0	0	0	0	0	0	0	0	9	2	5	-2
7	B.L.	Male	61	46	0	0	0	0	0	2	2	0	0	0	12	3	4	-5
8	B.L.			44	0	0	0	0	0	0	0	0	0	0	10	6	4	0
9	B.J.	Male	72	13	0	0	0	0	0	0	0	0	0	0	6	4	0	-2
10	A.P.	Female	47	21	0	0	0	0	0	0	0	0	0	0	10	4	4	-2
11	B.G.	Female	57	43	0	0	0	0	0	0	0	0	0	0	9	3	4	-2
12	A-C. H.	Female	41	45	0	0	0	0	0	0	0	0	0	0	9	5	3	-1
13	B.W.	Male	51	23	0	0	0	0	0	0	0	0	0	0	12	6	5	-1
14	K.J.	Female	46	36	0	0	0	0	0	0	0	0	0	0	9	2	7	0
15	G-M.L.	Female	49	36	0	0	0	0	0	0	0	0	0	0	6	3	3	0
16	K.J.	Male	50	22	0	0	0	0	0	0	0	0	0	0	6	4	4	2
17	B-M.H.	Female	42	17	0	0	0	0	0	0	0	0	0	0	6	4	5	3
18	S.J.	Male	46	12	0	0	0	0	0	0	0	0	0	0	8	2	3	-3
19	J.K.	Female	34	26	0	0	0	0	0	0	0	0	0	0	12	1	7	-4
20	B.S.	Male	51	14	0	0	0	0	0	0	0	0	0	0	9	3	6	0
	mean		51,1												8,9	3,1	4,9	-1,0
	SD		9,4												2,3	1,7	2,1	2,0
	Range		34 - 72												6 - 12	1 - 6	0 - 9	-5 - 3

PPD= Probing Pocket Depth; PAL= Probing Attachment Level; SD= Standard Deviation; w= Weeks; m= Months
*= Position of Gingival Margin in relation to Pre-surgical Level (neg. value = Recession)

Table 2. Clinical assessments of 12 treated furcation degree II defects in 10 patients. 6-month Evaluation

	Patient	Sex	Age	Tooth	Gingival Condition Index (0-3)					Exposure of device (mm)					PPD Initial (mm)	PPD Residual (mm)	PAL-V Gain (mm)	PAL-H Gain (mm)	Furcation at 6-months	Position of Gingival Margin* (mm)
					2w	1m	2m	3m	6m	2w	1m	2m	3m	6m						
1	U.L.	Male	41	46b	0	0	0	0	0	0	0	0	0	0	5	3	2	2	closed	0
2	U.L.			47b	0	0	0	0	0	0	0	0	0	0	9	3	5	4	closed	-1
3	G.S.	Female	44	26b	0	0	0	0	0	0	0	0	0	0	8	4	3	4	closed	1
4	S.D.	Female	38	46b	0	0	0	0	0	0	1	0	0	0	5	4	2	2	degree I	1
5	S.D.			47b	0	0	0	0	0	0	0	0	0	0	4	4	1	2	degree I	1
6	R.S.	Male	46	36b	0	0	0	0	0	0	0	0	0	0	5	3	3	4	closed	0
7	U.L.	Male	42	37b	0	0	0	0	0	0	0	0	0	0	6	4	2	3	degree I	0
8	A.S.	Male	58	47b	0	0	0	0	0	0	1	0	0	0	6	3	3	3	degree I	0
9	G.A.	Male	39	46l	0	0	0	0	0	0	0	0	0	0	4	1	5	3	closed	2
10	R.N.	Male	56	16m	0	0	0	0	0	0	0	0	0	0	6	2	2	2	degree I	-2
11	M.R.	Female	47	37b	0	0	0	0	0	0	0	0	0	0	6	2	4	4	closed	0
12	A.A.	Male	36	17b	0	0	0	0	0	2	2	2	0	0	9	3	6	4	closed	0
	mean		44,7												5,9	3,0	3,2	3,1		0,2
	SD		7,3												1,6	1,0	1,5	0,9		1,0
	Range		36 - 58												4 - 9	1 - 4	1 - 6	2 - 4		-2 - 2

PPD= Probing Pocket Depth; PAL= Probing Attachment Level (V= Vertical; H= Horizontal); SD= Standard Deviation; w= Weeks; m= Months
*= Position of Gingival Margin in relation to Pre-surgical Level (neg. value = Recession)

CLAIMS

1. An element for controlled tissue regeneration, comprising at least one member having opposite sides, and at least one spacer means for separating said member on at least one side thereof from an adjacent surface, said member having a ligature for anchoring the ligature to the tooth, c h a r a c t e r i z e d in that the element comprises anchoring means for the ligature engaging the ligature at positions spaced longitudinally of the ligature.

2. An element as claimed in claim 1 wherein end portions of said ligature extend freely from said anchoring means.

3. An element as claimed in claim 2 wherein said ligature is displaceable longitudinally in relation to said anchoring means.

4. An element as claimed in claim 3 wherein said anchoring means comprises undercut notches receiving the ligature therein the entrance of said notches being narrower than the thickness of the ligature but can be widened resiliently to allow passage of the ligature into the notch.

5. An element es claimed in claim 3 wherein the anchoring means comprises a helically wound strip forming a passage for the ligature.

6. An element as claimed in claim 3 wherein said anchoring means comprises a tube forming a passage for the ligature and having notches mutually spaced along the tube.

7. An element as claimed in claim 2 wherein said ligature is fixedly mounted to said element by said anchoring means engaging the ligature.

8. An element as claimed in claim 7 wherein said anchoring means comprises resilient members forming notches, said ligature being received in said notches under resilient deformation of said members.

9. An element for controlled tissue regeneration, comprising at least one member having opposite sides, and at least one spacer means for separating said member on at least one side thereof from an adjacent surface, c h a r a c t e r i z e d in that said spacer means comprises a mesh, a net, or a knitted, woven or non-woven fabric.

10. An element as claimed in claim 9 wherein said mesh, net, or knitted woven or non-woven fabric forms spacer means between two sheets of a sandwich or laminate structure.

11. An element as claimed in claim 9 wherein said mesh, net, or knitted woven or non-woven fabric forms spacer means at at least one side of the element.

12. An element for controlled tissue regeneration, comprising at least one member having opposite sides, and at least one spacer means for separating said member on at least one side thereof from an adjacent surface, c h a r a c t e r i z e d in that said element forms a self-supporting central portion and a marginal portion surrounding said central portion, for sealing engagement with a bone surface surrounding a bone defect covered by said central portion.

13. An element as claimed in claim 12 wherein said central portion is domeshaped.

14. An element as claimed in claim 13 wherein said central and marginal portions form one sheet of a laminate or sandwich structure comprising a second sheet and spacer means between said one sheet and said second sheet, said second sheet being malleable to follow the shape of said central portion.

15. A method for providing selected influence on tissue regeneration, comprising the step of providing a space for tissue growth between an implanted element and an adjacent bone tissue, c h a r a c t e r i z e d in that a seal is provided between said element and said adjacent bone tissue.

16. A method as claimed in claim 15 wherein said seal is provided around a bone defect.

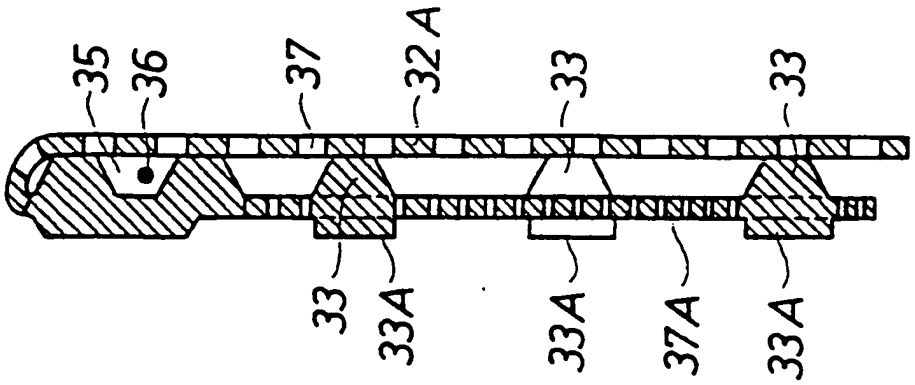


FIG. 3

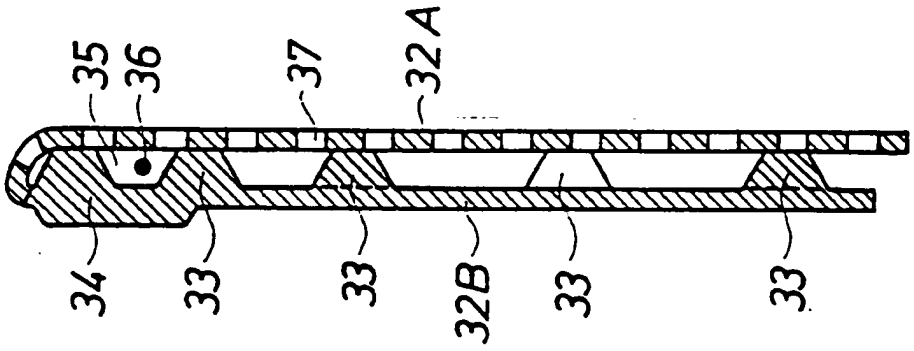


FIG. 2

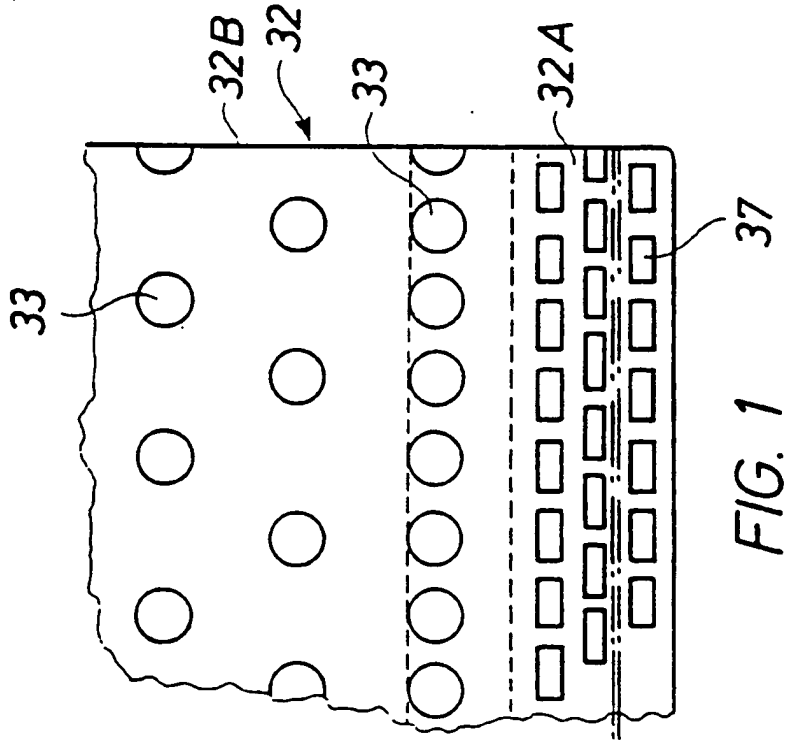


FIG. 1

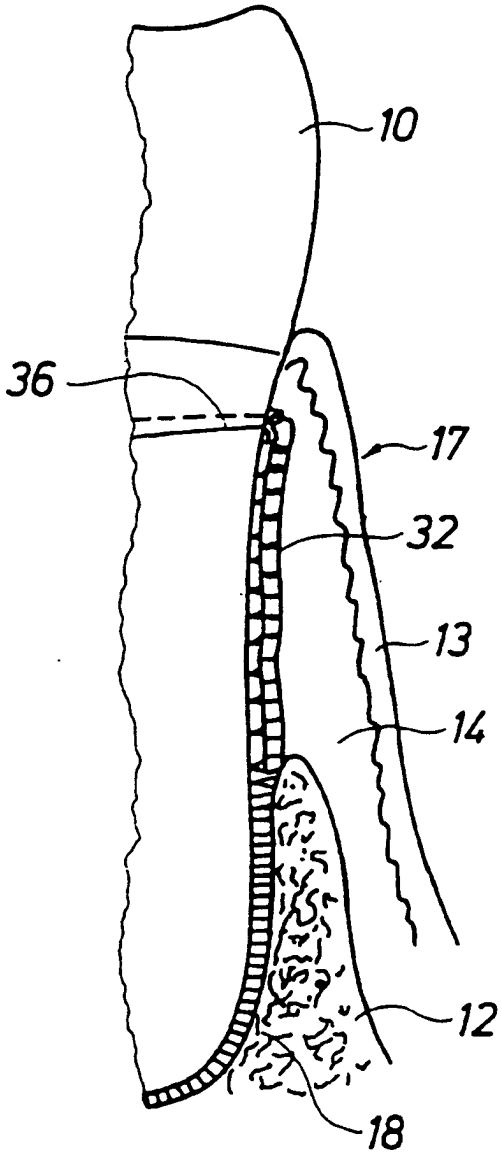


FIG. 4

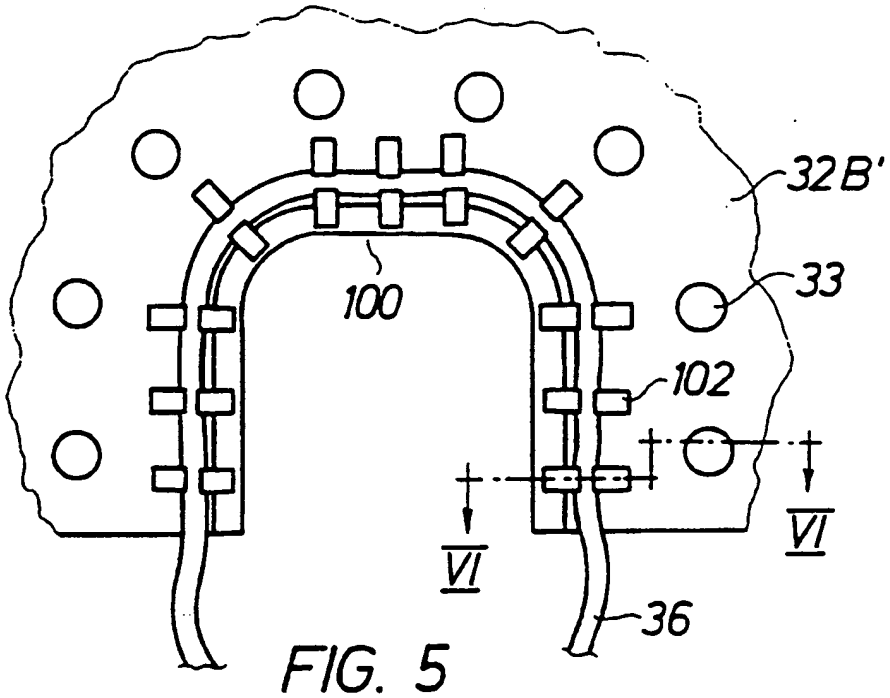


FIG. 5

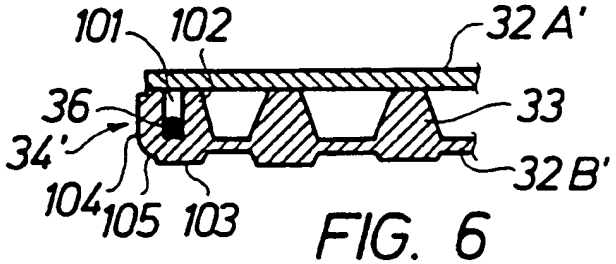


FIG. 6

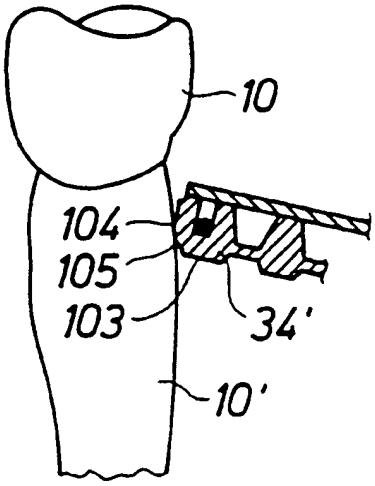


FIG. 7

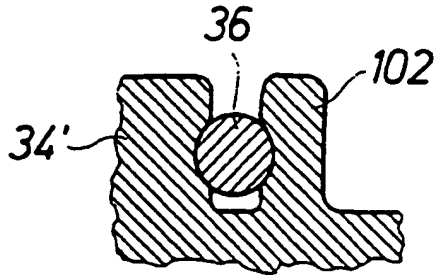


FIG. 8

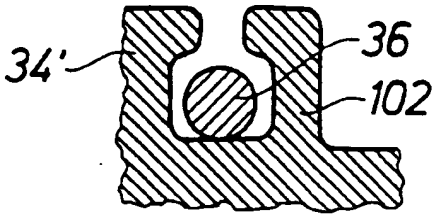


FIG. 9

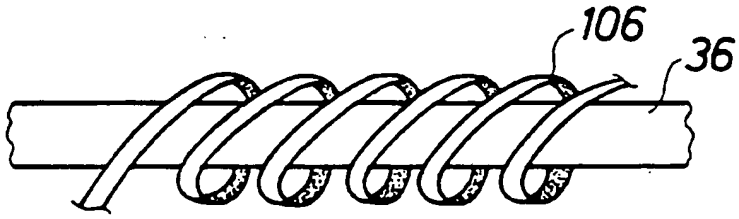


FIG. 10

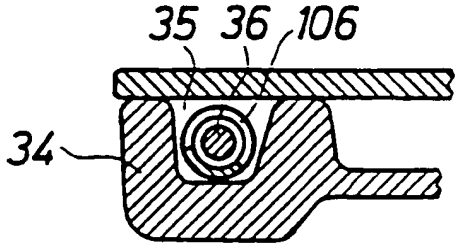


FIG. 11

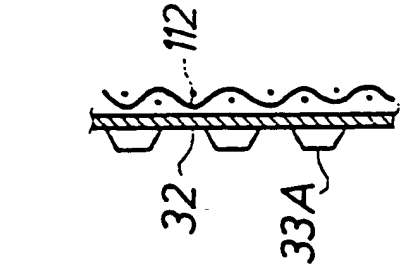


FIG. 16

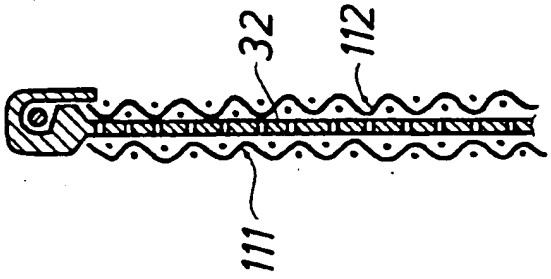


FIG. 15

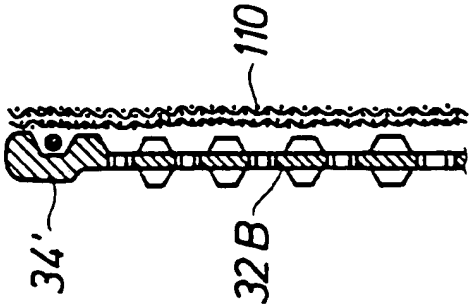


FIG. 14

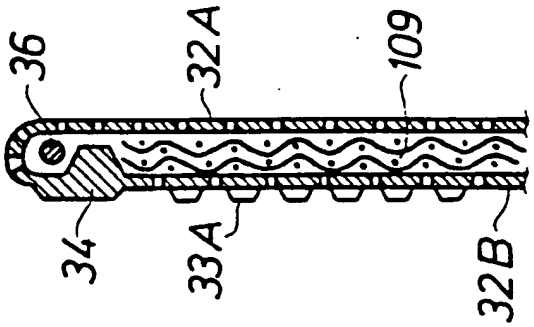


FIG. 13

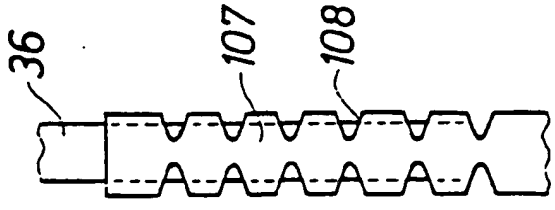


FIG. 12

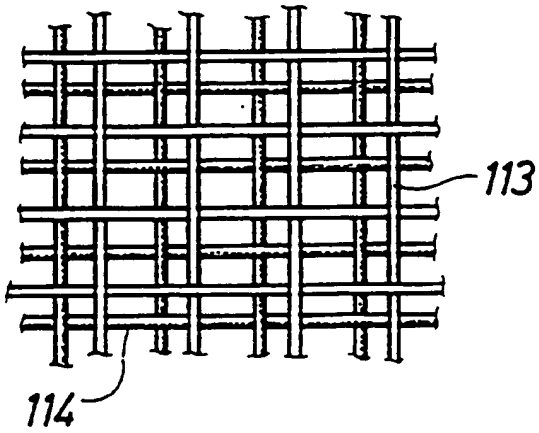


FIG. 17

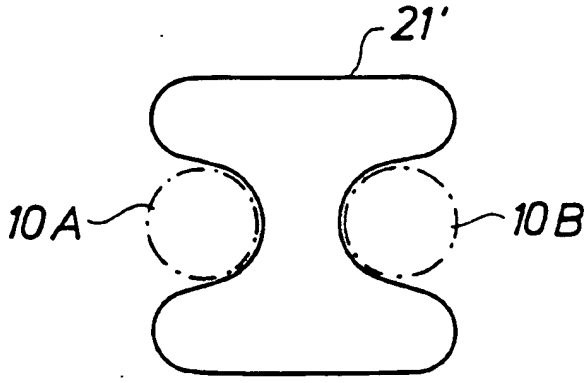


FIG. 18

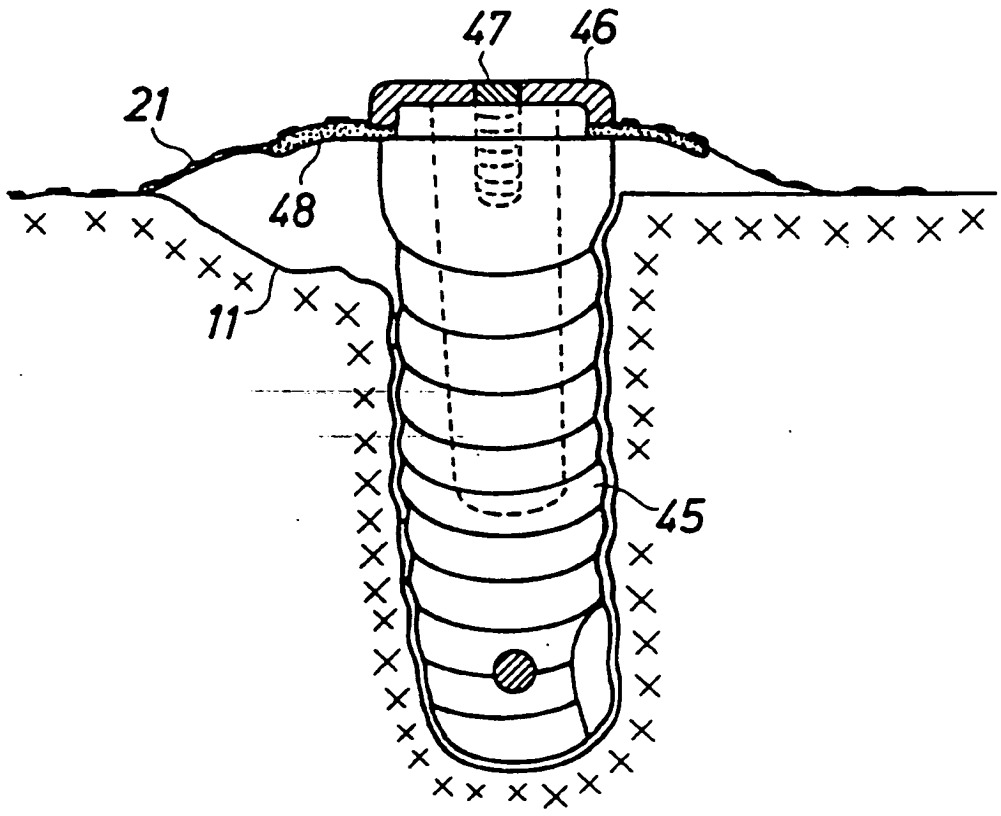


FIG. 19

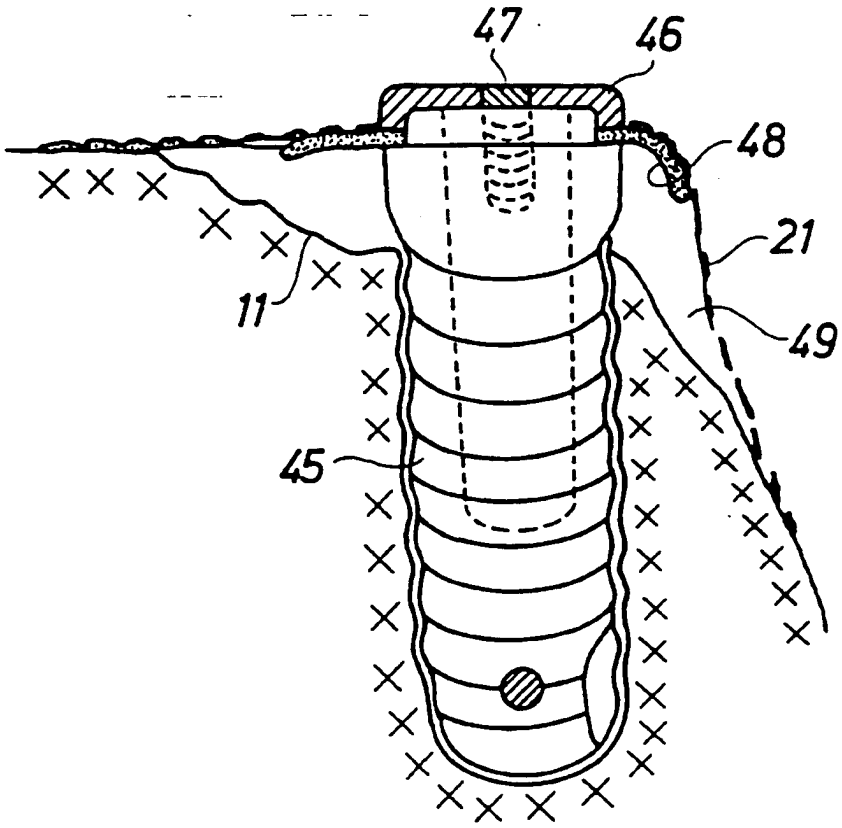


FIG. 20

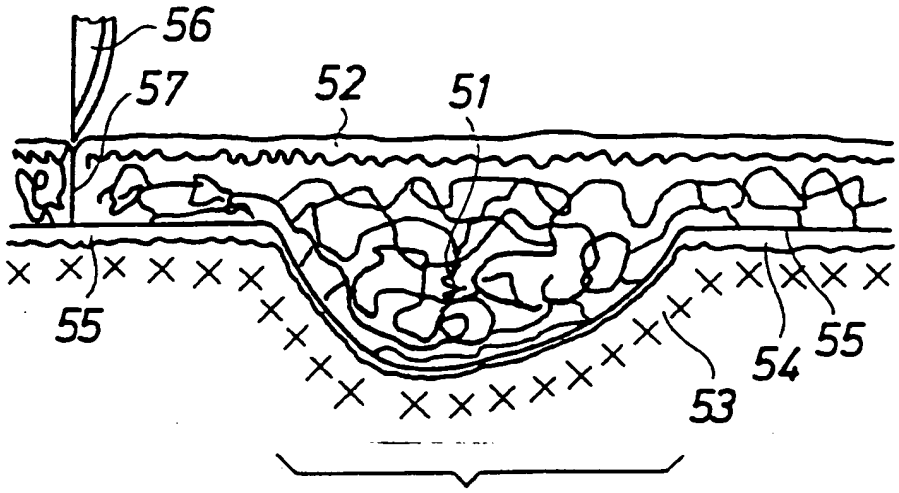


FIG. 21

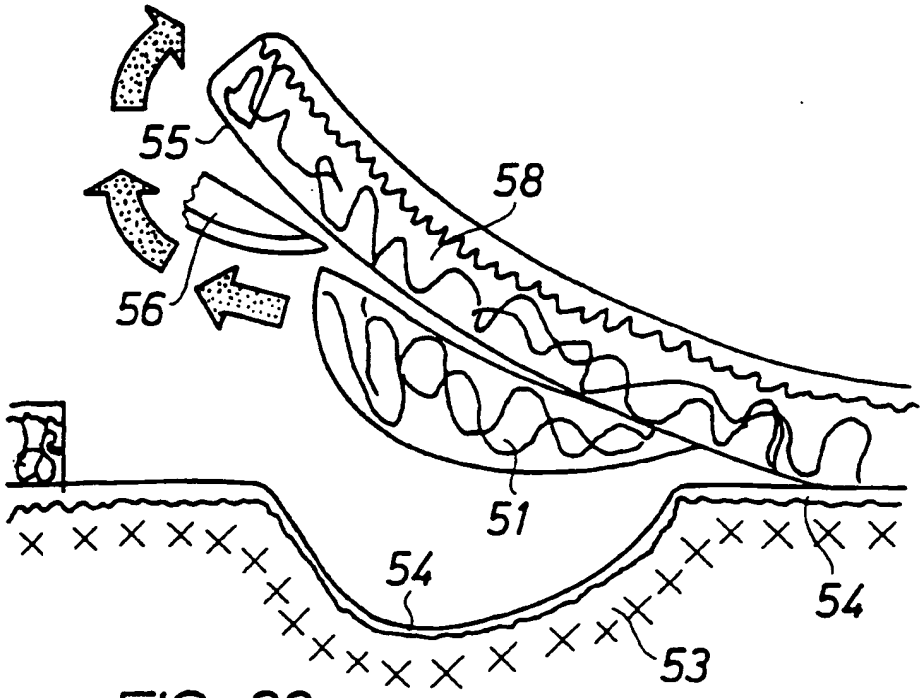


FIG. 22

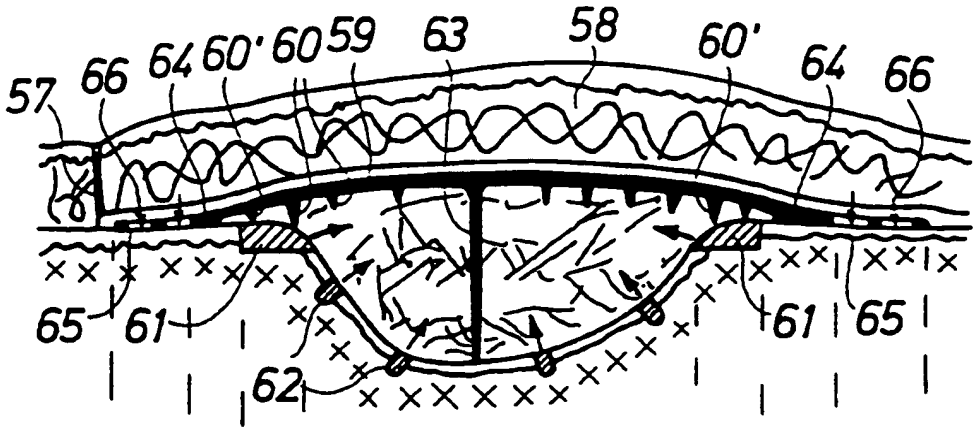


FIG. 23

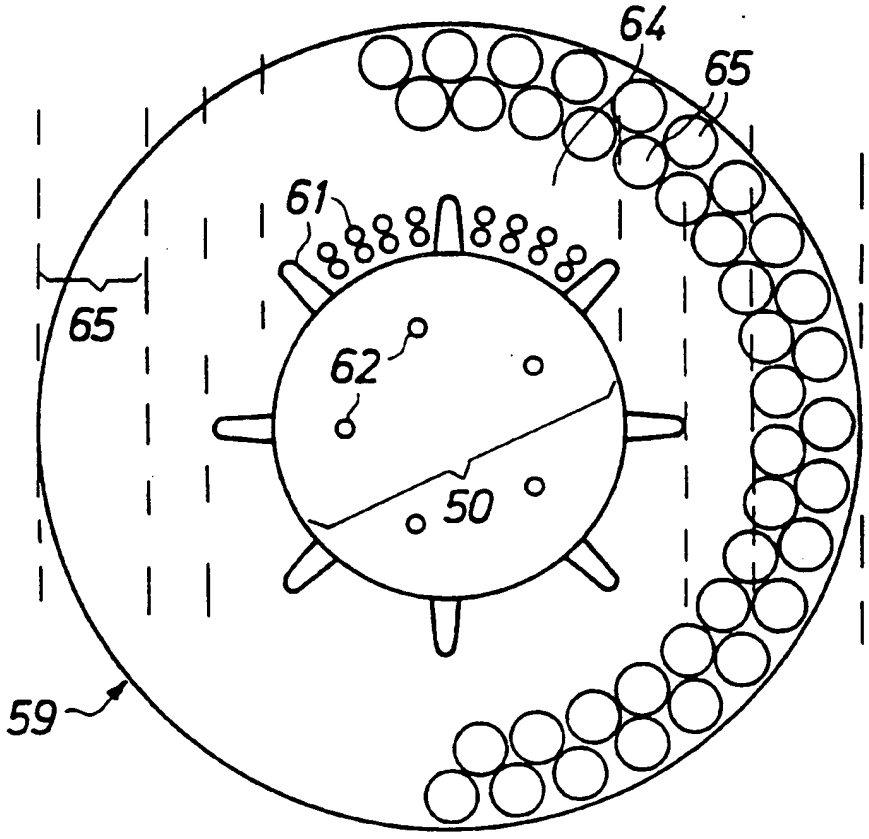


FIG. 24

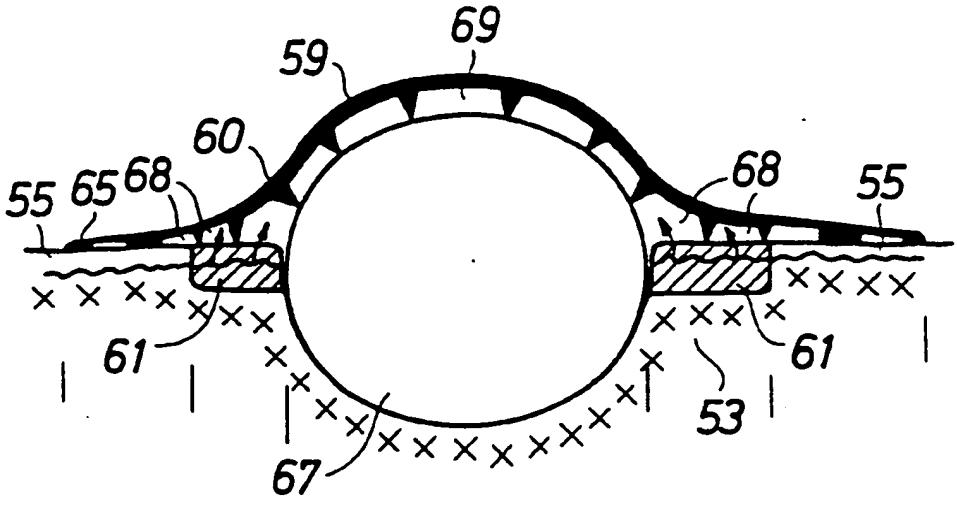


FIG. 25

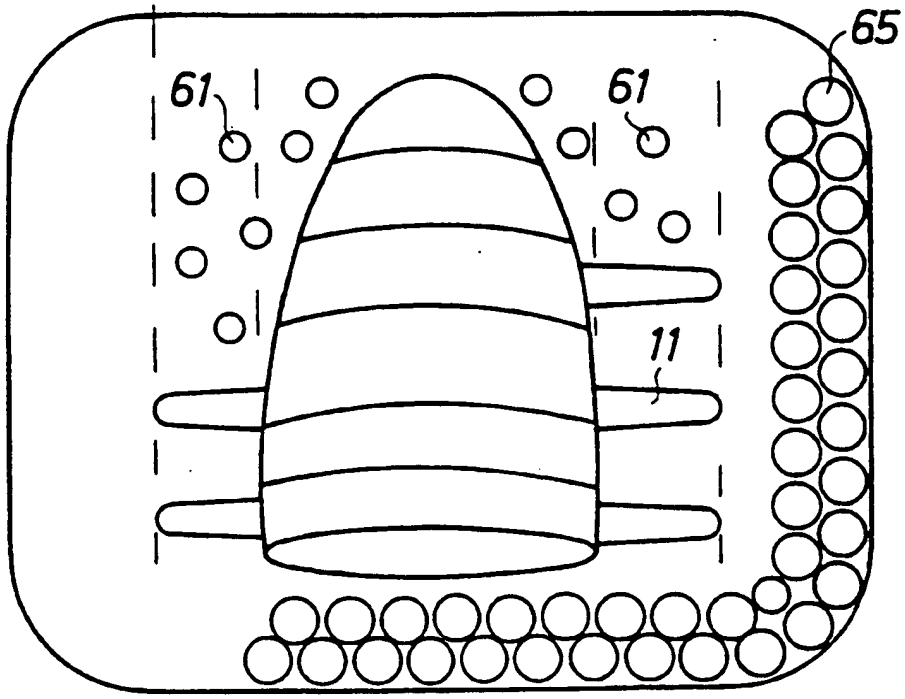


FIG. 26

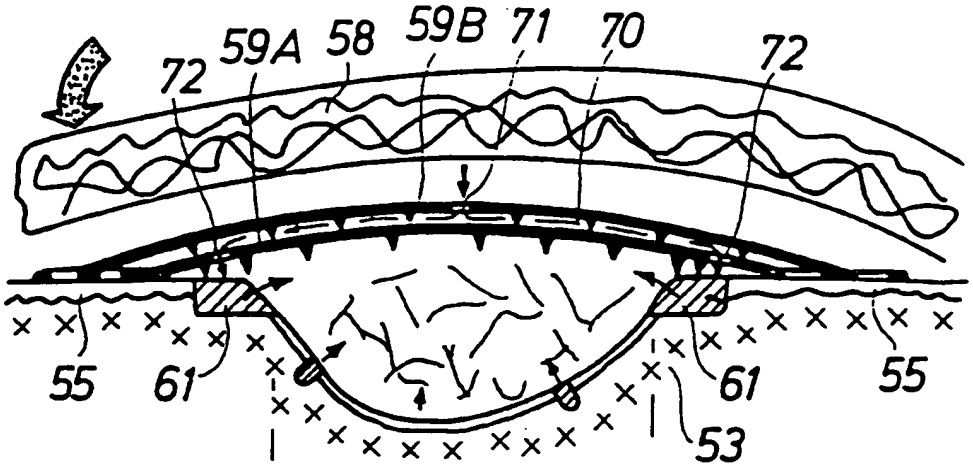


FIG. 27

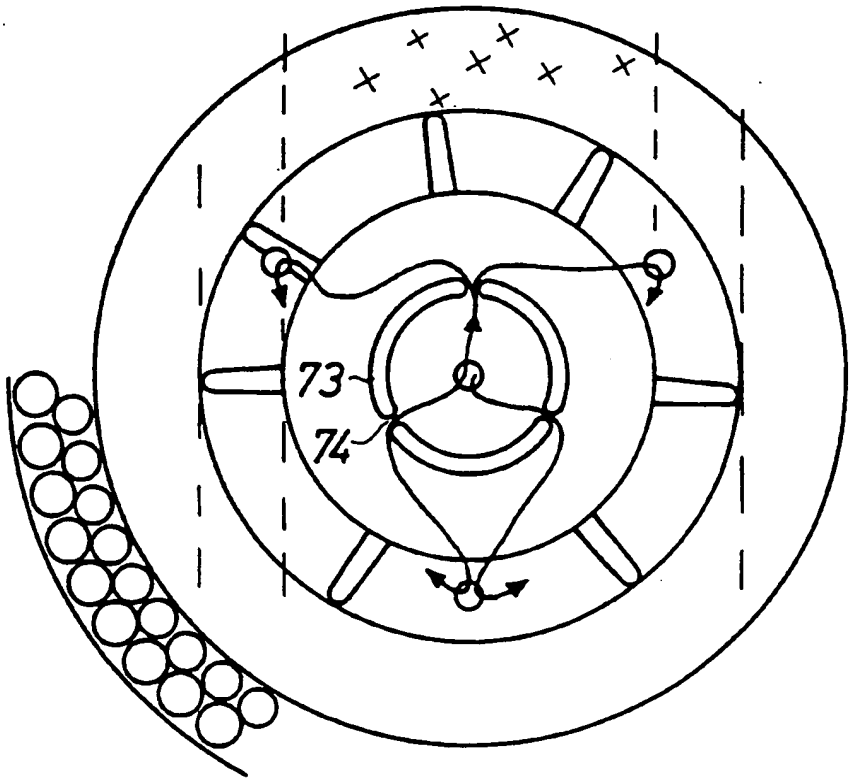


FIG. 28

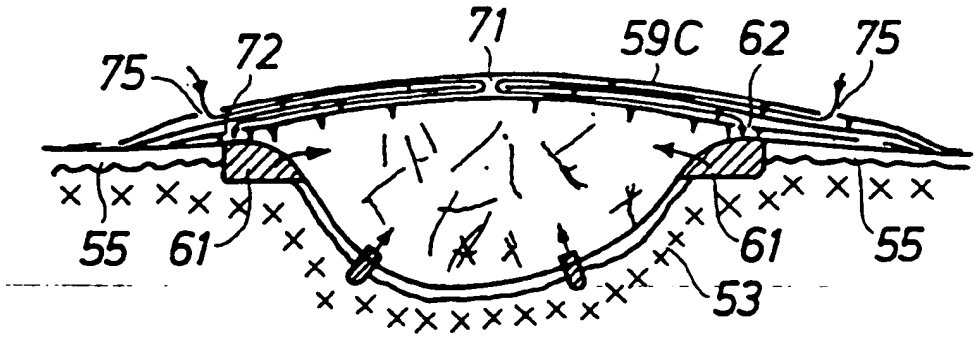


FIG. 29

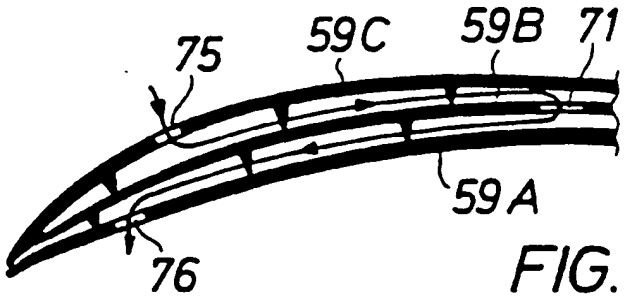


FIG. 30

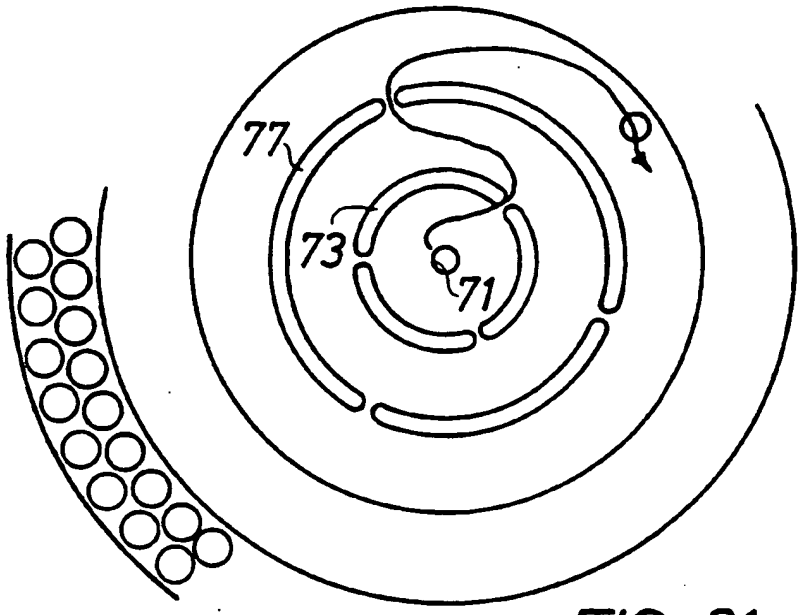


FIG. 31

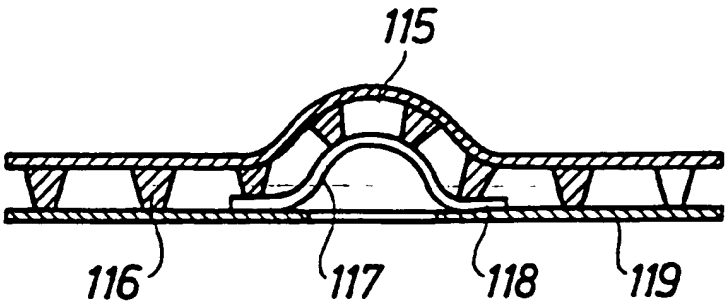


FIG. 32

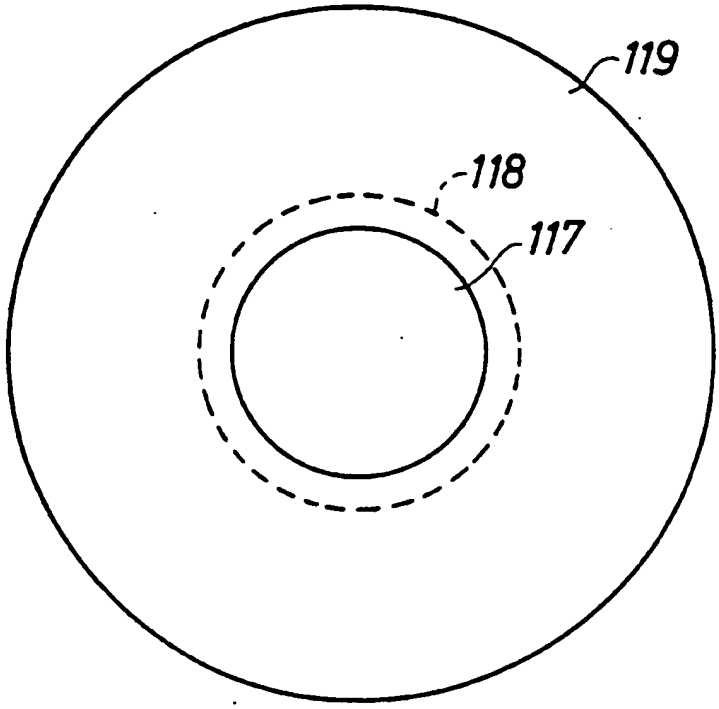


FIG. 33